REMARKS

The Applicant respectfully requests reconsideration of the objections and rejections set forth in the Final Office Action dated February 24, 2004, and the Examiner Interview dated April 22, 2004, for the above-identified patent application.

The Rejection under 35 U.S.C §112:

Claims 1-3, 5, 6, 66 and 78 stand rejected over 35 USC §112, second paragraph, as being indefinite for the reasons set forth in the Office Action. The Applicants have amended these claims in the manner suggested by the Examiner. Specifically, the communication structure, the aspiration actuator and dispensing actuator are now positively claimed.

Moreover, regarding the concern that the claimed invention would no longer constitute a valve, the Applicants respectfully disagree, but nonetheless have amended the preamble to be "A hydraulic hybrid valve system to enable transfer of a liquid sample slug from a reservoir to a test site on a substrate surface". Hence, it is now a valve system including a valve that enables liquid manipulation. Accordingly, withdrawal of the §112 rejection is respectfully requested.

The Rejection under 35 U.S.C §102(b):

The Examiner has rejected claims 1-3, 59 and 63-65 under 35 USC §102(b) as being anticipated by new reference Kenny, U.S. Patent No. 4,461,328. In view of the above-indicated amendments and the forgoing remarks, the Applicants respectfully disagree.

Briefly, exemplary claim 1 now recites a hydraulic hybrid valve system to enable transfer of a liquid sample slug from a reservoir to a test site on a substrate surface. The valve system includes a communication structure having a dispensing

orifice; an aspiration actuator; a dispensing actuator; and a valve assembly movable between an aspiration condition and a dispensing condition. The valve system further includes a distribution manifold device providing a liquid aspiration conduit containing a driving liquid and having a first aspiration port and a second aspiration port. The first aspiration port is configured for liquid communication with the aspiration actuator, while the second aspiration port is in selective liquid communication with the valve assembly to selectively aspirate a liquid sample slug from the reservoir through the dispensing orifice of the communication structure. A discrete sample path is defined containing the driving liquid and extending from the dispensing orifice of the communication structure and through at least a portion of the manifold device for liquid communication with the valve assembly. When the valve assembly is in the aspiration condition, the manifold device further provides a liquid dispensing conduit containing a driving liquid and having a first dispensing port for liquid communication with the dispensing actuator, and a second dispensing port in selective liquid communication with the valve assembly to selectively dispense at least one droplet of the liquid sample slug from the dispensing orifice of the communication structure when the valve assembly is in the dispensing condition. In the aspiration condition, the sample path is out of liquid communication with the dispensing actuator and, in the dispensing condition, the sample path is out of liquid communication with the aspiration actuator.

Accordingly, the present invention provides a complete hydraulic hybrid valve system that enables aspiration into and precision dispensing of the liquid sample from dispensing orifice in minute or micro volumes. By containing a driving liquid in both the aspiration conduit and the dispensing conduit, a near liquid-to-liquid interface is created between the driving liquid and the sample liquid slug, forming a hydraulically

driven system that permits precision fluid aspirating and dispensing. As set forth in the present pending application at page 25, lines 11-12:

> [The] mobile phase fluid 85, 86 [is] supplied to the aspiration actuators 21 and the dispensing actuators 22 as a driving fluid.

Since this hydraulic arrangement is nearly a liquid-to-liquid interface, as opposed to the air-to-liquid interface of the cited references, there is no air compression. Hence, the pressure pulse caused by the aspirating and dispensing actuators can be easily transferred across the interface between the driving liquid to the sample slug contained in the sample path. Consequently, amongst other factors, the aspiration and dispensing energy output by the actuators can be concentrated on the aspiration and dispensing procedures to aspirate and dispense precise amounts in very minute quantities. In other words, due to the combination of the hydraulic configuration and the precision actuators, the present invention has:

> the ability to deliver independent, short-duration, pressure pulses associated with ink-jet print valves enables the non-contact tunable delivery of reagent sample volumes in the range of about $(10)^{10}$ to about $(10)^{-12}$ liters.

Kenny, in contrast, discloses a multi-component pipetting device aspirating into a well of the conical pipetting tube 4 of a tray 3. Referring to the embodiment of FIGURES 5 and 6, a pipette device 2 is removably mounted to tray 3 that provides an interconnection 36 mounted to one end of a flexible hose 38. The other end of the flexible hose is coupled to valve 52, which in turn is connected through flexible lines 54 and 56 to a pressure source and a vacuum source, respectively. A hydrophobic filter sheet 20 (col. 2, lines 18-22 and 61-60) is disposed over the wells of the pipetting tubes 4, separating them from the cavity formed by the top plate 30 and the plate 27. Accordingly, the device of Kenny can only dispense aqueous (non-hydraulic) fluids since a non-aqueous fluid flowing through the hydrophobic filter

would damage it. Moreover, a dispensing gas must be employed on the other side of the filter to drive the process and permit the passage of gas (col. 2, lines 30-32), as opposed to utilizing a hydraulic driving means, such as the driving liquid of the present invention.

Accordingly, since Kenney is only for a non-hydraulic (air/liquid dispensing) driving application, the volumes of sample aspirated and dispensed cannot be accurately controlled. This is due in part to the fact that using a compressive gas as a driving fluid, the gas compresses and expands, and thus cannot accurately aspirate and dispense liquids.

Moreover, the hydrophobic design of Kenny requires that the volumes of sample aspirated into and dispensed from the wells of the tubes 4 are thus fixed (col. 2, lines 62-67). The aqueous fluid is drawn into the wells of the tubes 4 until it reaches the hydrophobic filter sheets 20 "which stops the upward movement of liquid in the tubes" (*Id.* at lines 64-65). An exact predetermined amount of liquid is thus contained, since otherwise you cannot determine the amount aspirated or dispensed in this device (*Id.* at lines 65-67). Consequently, the arrangement of Kenny is not conducive for accurate, non-contact aspiration and dispensing in variable volumes since the compressive gas driving fluid is not capable of drop ejection in an accurate, reproducible manner.

The present invention, by comparison, is capable of complete hydraulic aspiration and dispensing, and in variable, reproducible amounts at very low volumes. Since the hydraulic application of the present invention employs driving fluids for aspiration and dispensing (Page 25, lines 10-20 of the present pending application), there is substantially nil volume of compression or expansion at the interface, allowing energy transfer there across that is directly transferred to the aspirated or dispensed sample.

The importance of this is that, unlike the non-hydraulic device of Kenney, accurate, reproducible dispensing can be performed, as well as delivering variable volume dispensing of non-aqueous fluids chemicals.

The device of Kenny also cannot dispense fluids of varying viscosities from the multiple wells since the gas pressure will typically cause the less viscous fluids to be dispensed first (i.e., less resistance) therefrom. Once the first well is empty, the gas will then all pass through that empty well and not dispense anymore fluids from the other wells.

The present invention, of course, is capable of allowing discrete on/off functionality, and can open one channel while the other is completely off. Hence, not only can variable volumes can be dispensed simultaneously, but the present invention can also simultaneously dispense fluids of different viscosities.

In view of the foregoing arguments and amendments, withdrawal of the §102 rejections is respectfully requested.

The Rejection under 35 U.S.C §103(b):

The Examiner has rejected claims 5-10 and 62-65 under 35 USC §103(a) as being unpatentable over Kenny, and further in view of Naono. In view of the above-indicated amendments and the forgoing remarks, the Applicants respectfully disagree.

Naono discloses a complex, multiple component device that is hydraulically driven by applying multiple valves to perform the functionality of the present invention. Accordingly, the applicant submits that it would be improper to combine the Non-Hydraulic device of Kenny with the Hydraulic driven device of Naono. Also, rotary-type switching valves of Naono do not function properly unless Hydraulically driven, and Naono discloses a flow through application as opposed to an aspirate/dispense model, as the present invention suggests. Hence, even if the

combination of Kenny and Naono could be combined, the arrangement would still be an aqueous only device, and would still be a fixed volume aspiration/dispensing system incapable of accurate fluid deliver in reproducible and minute amounts..

In view of the foregoing arguments and amendments, withdrawal of the §103(a) rejection is respectfully requested.

Conclusion

In light of the above amendments and remarks, the Applicants respectfully request that the Examiner reconsider this application with a view towards allowance. It is believed that all claims now pending and all Currently Amended claims fully and patently define the subject invention over the cited art of record and are in condition for allowance.

If the Examiner has any questions concerning this case, the Examiner is respectfully requested to contact Michael L. Louie at (510) 843-6200.

The Commissioner is hereby authorized to charge any additional fees, including any extension fees, which may be required or credit any overpayment directly to the account of the undersigned, No. 50-0388 (Order No. INVDP001).

Respectfully submitted,
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